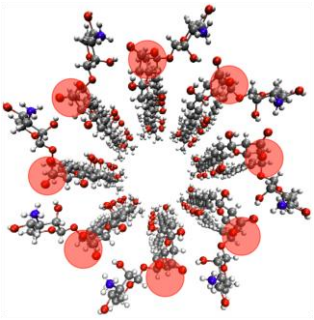
Exploring the Mechanism of Ion Selectivity in the Amphotericin B Ion Channel

Stephen Davis and Martin Burke.

In cell membranes, Amphotericin B (AmB) is known to form ion channels exhibiting an ion selectivity of 7:1 K^+ : Cl^-. According to molecular modeling studies, the C41 carboxylate is positioned at the channel entrance (Figure 1). A ring of carboxylates is hypothesized to cause a local negatively charged area, concentrating K^+ ions and explaining the observed ion selectivity. This hypothesis can be tested by synthesizing derivatives of AmB in which the carboxylate is replaced with either a methyl group (**1**), or an amine (**2**). Derivative **1** lacks charge and therefore should exhibit diminished cation selectivity. Amine **2** could form a positively charged ring, potentially inverting the ion selectivity, thus creating an anion selective channel.



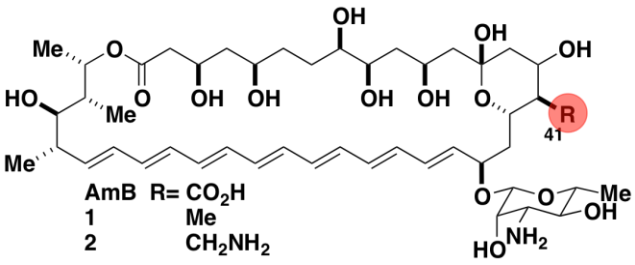


Figure 1: Aerial view of AmB channel, carboxylate highlighted in red.